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Research Letter

Prenatal diagnosis and molecular cytogenetic characterization of mosaicism for a small supernumerary marker chromosome derived from chromosome 21

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Dear Editor,

A 34-year-old woman, primigravid underwent amniocentesis at 18 weeks of gestation because of advanced maternal age. Amniocentesis revealed a karyotype of 47,XY,+mar[8]/46,XY[16]. Among 24 colonies of cultured amniocytes, eight colonies had a karyotype of 47,XY,+mar, while the rest 16 colonies had a karyotype of 46,XY. The small supernumerary marker chromosome (sSMC) was bisatellited (Fig. 1). The parental karyotypes were normal. Array comparative genomic hybridization (aCGH) analysis on the DNA extracted from cultured amniocytes by Roche ISCA Plus Cytogenetic Array (Roche NimbleGen, Madison, WI, USA) revealed no genomic imbalance. Metaphase fluorescence *in situ* hybridization (FISH) analysis using the Acro p-arm DNA FISH probe (Abbott, Abbott Park, IL, USA) and the CEP13/21 FISH probe (Cytocell Inc, Adderbury, Oxfordshire, UK) revealed a result of +mar .ish der(13/21)(D13/21Z1+, acro-p++)[2/20], indicating that the sSMC was derived from chromosome 13/21 (Fig. 2). The Acro p-arm DNA FISH probe is designed in spectrum orange fluorophore to hybridize to the p12-p13 region of the acrocentric chromosomes 13, 14, 15, 21 and 22. The CEP13/21 FISH probe is designed in spectrum fluorescein isothiocyanate (FITC) (green) fluorophore to hybridize to the D13/21Z1 region. Polymorphic DNA marker analysis on the DNA extracted from cultured amniocytes by quantitative fluorescent polymerase chain reaction (QF-PCR) using the informative marker of D21S16 (21q11.2) showed two alleles with a ratio of 1.8:1 in the proband comparing with the ratio 1:1 in the normal control (Fig. 3), indicating the sSMC was derived from chromosome 21. Prenatal ultrasound findings were unremarkable. The parents elected to continue the pregnancy, and a 3060-g phenotypically normal male baby was delivered uneventfully at 39 weeks of gestation. Cytogenetic analysis of cord blood revealed a karyotype of 47,XY,+mar[23]/46,XY[17].

An sSMC is a small supernumerary marker chromosome that is equal in size or smaller than a chromosome 20 and cannot be characterized by conventional cytogenetics [1–3]. sSMCs occur in 0.044% of newborn infants and in 0.075% of prenatal cases [1,3,4]. About 70% of sSMCs are caused by a *de novo* event [5], about 70% of sSMCs are derived from acrocentric chromosomes [1,6], and about 70% cases of *de novo* sSMCs are associated with no phenotypic abnormalities [4]. In a study of 112 sSMCs with FISH results, Crolla et al. [7] found sSMC(15) in 34.8%, sSMC(13/21) in 12.5%, sSMC(14) in 11.6% and sSMC(22) in 8.9%. Crolla et al. [7] suggested that an sSMC derived from an acrocentric chromosome carries a 7% risk of phenotypic abnormalities. We previously reported prenatal diagnosis and molecular cytogenetic characterization of sSMCs derived from acrocentric chromosomes such as 15, 21 and 22 [8–10]. Here,

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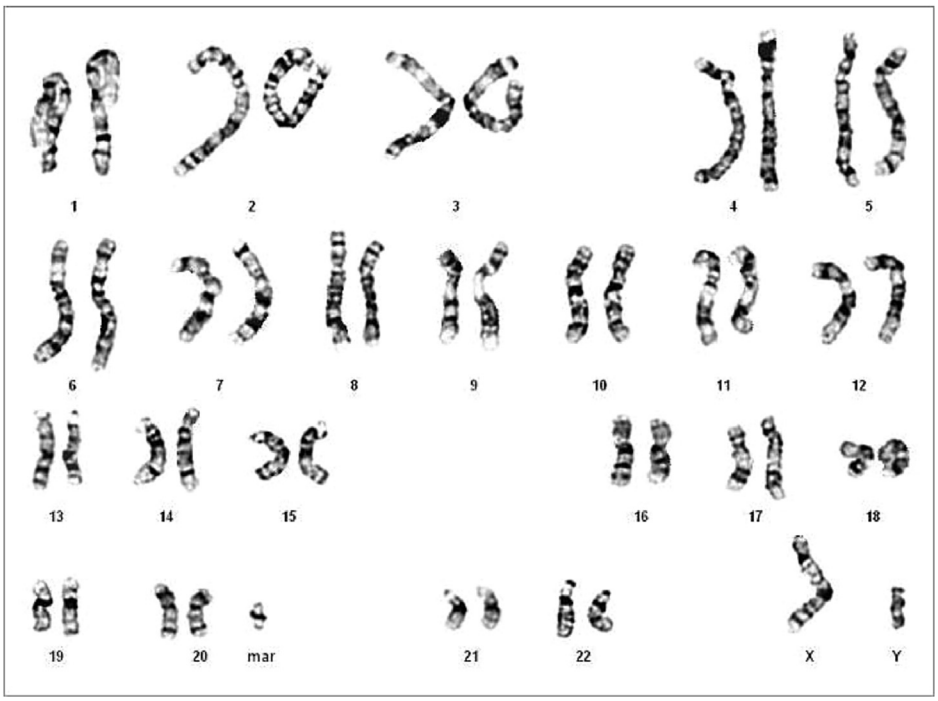

Fig. 1. A karyotype of 47,XY,+mar. mar = marker chromosome.

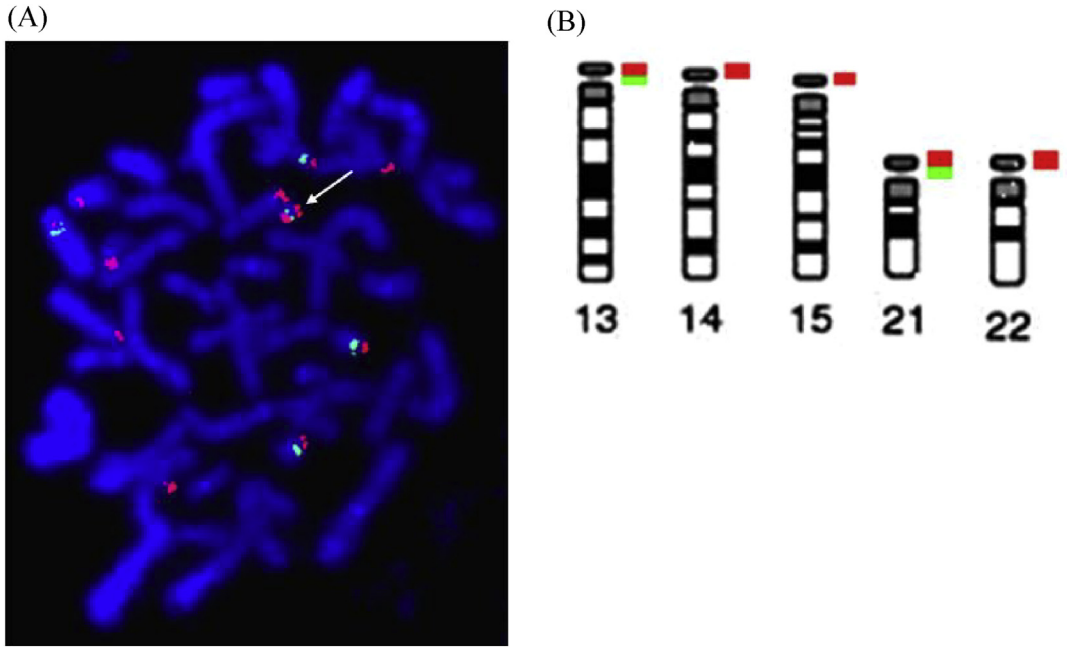

Fig. 2. (A) Fluorescence *in situ* hybridization (FISH) analysis using the Acro p-arm DNA FISH probe designed in spectrum orange fluorophore to hybridize to the p12-p13 region of the acrocentric chromosomes 13, 14, 15, 21 and 22 and the CEP13/21 FISH probe designed in spectrum fluorescein isothiocyanate (FITC) (green) fluorophore to hybridize to the D13/21Z1 region shows two red signals and one green signal in the marker chromosome (arrow), indicating a bisatellited marker chromosome derived from chromosome 13/21. (B) The ideogram shows the labeling colors and locations of the FISH probes of Acro p-arm probe (orange) and CEP13/21 probe (green).

we additionally reported prenatal diagnosis and molecular cytogenetic characterization of an sSMC(21) by the FISH probe of CEP13/21 and polymorphic DNA marker analysis by QF-PCR. We previously reported prenatal diagnosis of an sSMC(21) by the FISH probe of CEP13/21 and SALSA multiplex ligation-dependent probe amplification (MLPA) P181 with a duplication of the 21q11.2 segment containing the *STCH* and *SAMSN1* genes. In this presentation, following a positive identification of sSMC(13/21) by the CEP13/21 (D13Z1/D21Z1) FISH probe, we used an alternative method of polymorphic DNA marker analysis for differential diagnosis of an sSMC(21) by choosing an informative marker of D21S16 (21q11.2). Our demonstration provides evidence for the usefulness of QF-PCR assay in rapid identification of an sSMC derived from chromosome 21.

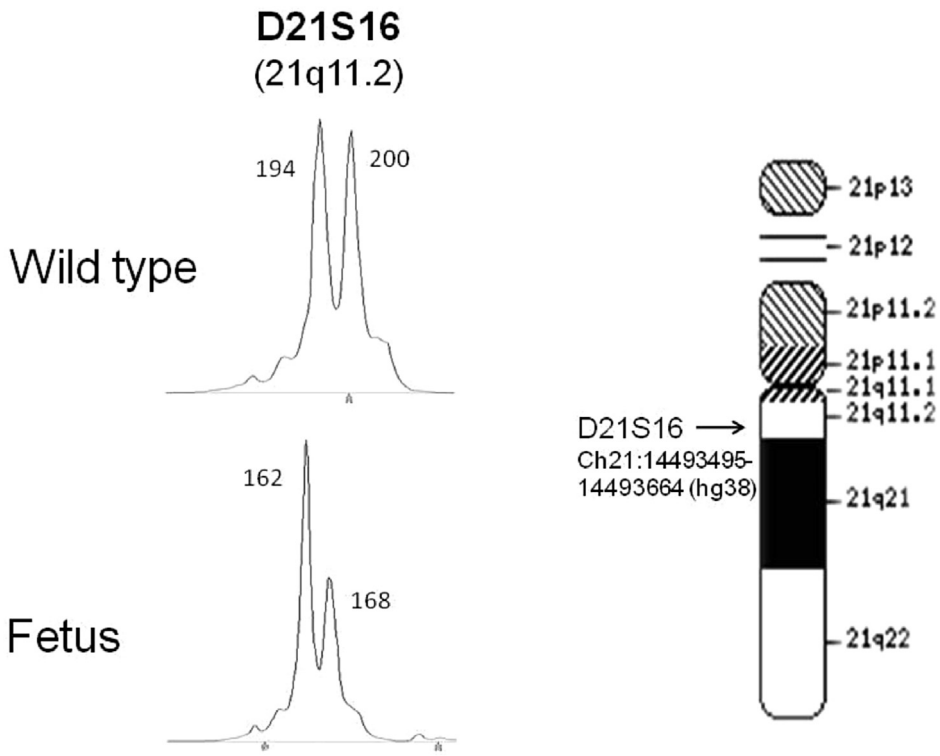

Fig. 3. Polymorphic DNA marker analysis on the DNA extracted from cultured amniocytes using the informative marker of D21S16 (21q11.2) shows two alleles with a ratio of 1.8:1 in the proband comparing with the ratio 1:1 in the normal control, indicating the marker chromosome is derived from chromosome 21.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

Acknowledgements

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